# REPORT DOCUMENTATION PAGE

*Form Approved*
*OMB No. 0704-0188*



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| 1. REPORT DATE *(DD-MM-YYYY)* | 2. REPORT TYPE | 3. DATES COVERED *(From - To)* |
|---|---|---|
| 17/3/2008 | Final Report | 3/1/04 - 2/28/07 |

**4. TITLE AND SUBTITLE**

Chemical/Radiation Hormesis Database, Evaluation of Hormetic Mechanisms and Their Biomedical and Risk Assessment Implications

**5a. CONTRACT NUMBER**

**5b. GRANT NUMBER**

FA9550-04-1-0104

**5c. PROGRAM ELEMENT NUMBER**

**6. AUTHOR(S)**

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**5d. PROJECT NUMBER**

0026492004

**5e. TASK NUMBER**

**5f. WORK UNIT NUMBER**

**7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)**

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**8. PERFORMING ORGANIZATION REPORT NUMBER**

ST:A122165/S13300001100000

**9. SPONSORING/MONITORING AGENCY NAME(S) AND ADDRESS(ES)**

AFOSR/NL
875 N Randolph St
Arlington VA 22203

**10. SPONSOR/MONITOR'S ACRONYM(S)**

AFOSR

**11. SPONSOR/MONITOR'S REPORT NUMBER(S)**

**12. DISTRIBUTION/AVAILABILITY STATEMENT**

Unlimited Release

AFRL-SR-AR-TR-08-0189

**13. SUPPLEMENTARY NOTES**

**14. ABSTRACT**

This project assessed the biomedical and toxicological literature for evidence of hormesis, its frequency in the literature and its underlying mechanistic foundation. This work was supported by the continued development of the hormesis database and the conduct of a high level international conference on hormesis held annually. Particular focus was given to the area of neuroscience and hormesis in the literature assessment. Fourteen manuscripts concerning hormesis and neuroscience have been accepted for publication in the journal Critical Reviews in Toxicology and will be published in 2008.

**15. SUBJECT TERMS**

| 16. SECURITY CLASSIFICATION OF: | | | 17. LIMITATION OF ABSTRACT | 18. NUMBER OF PAGES | 19a. NAME OF RESPONSIBLE PERSON |
|---|---|---|---|---|---|
| a. REPORT | b. ABSTRACT | c. THIS PAGE | | | Edward J. Calabrese |
| Final | | | | | 19b. TELEPHONE NUMBER *(Include area code)* 413-545-3164 |

**Period Covered:** March 1, 2004 – February 28, 2007

**Title of Proposal:** Chemical/Radiation Hormesis Database, Evaluation of Hormetic Mechanisms and Their Biomedical and Risk Assessment Implications

**Grant Number:** FA9550-04-1-0104

**Institution:** University of Massachusetts, Amherst Massachusetts

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**Publications:**

**2007**

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**List of Personnel Supported by this Grant:**

Hannah Allaben (hourly) – 6/18/06-8/28/06
Robyn Blain (hourly) – 9/1/05-2/24/07
Edward Calabrese (PI) – 5/28/06-9/1/06
Ben DiTrolio (hourly) – 6/18/06-9/1/06
Brenda Gomex (hourly) – 7/16/06-9/1/06
Wilson Poon (hourly) – 9/3/06-2/24/07

Paula Goodhind (100%) – 9/1/05-2/24/07
George Hoffmann (hourly) – 1/1/06-2/24/07
Julia Ryan (hourly) – 7/31/05-4/1/06
John S. Staudenmayer – 6/4/06-7/15/06

**Invention/Patents/Discoveries:** None

**Collaborators/Consultants:** Two statisticians (JWS/EJS) and a mechanistically oriented genetic toxicologist (GRH) are working on analysis of several large high through-put databases of anti-tumor and anti-bacterial agents in order to compare the hormesis dose-response model and the threshold model for low-dose prediction. These include:

John W. Staudenmayer, Ph.D. – Mathematics and Statistics; University of Massachusetts; Amherst, MA 01003

Edward J. Stanek III, Ph.D. – Department of Biostatistics and Epidemiology; School of Public Health; University of Massachusetts; Amherst, MA 01003

George R.Hoffmann, Ph.D. – College of the Holy Cross; Biology; Worcester, MA 01610

**Honors or Awards**: None

**Key Findings/Results/Accomplishments:**

Using a large NCI cell toxicity database with 57,000 dose responses and approximately **2,200** chemicals we demonstrated that the threshold dose response model was unable to provide accurate and reliable predictions of responses in the low dose zone. During the same testing procedure the hormetic dose response model was able to provide accurate and reliable estimations of responses in the low dose zone. More detailed analyses revealed that essentially all chemicals satisfying entry criteria for evaluation induce responses consistent with the hormesis dose response model. We believe that this is a very significant finding since it not only challenges the accuracy of the most widely used model in toxicology but also provides evidence to support an alternative model. The next step in our research is to assess whether the threshold and hormetic dose response models can be similarly tested in other large high through-put databases in order to be able to generalize the above findings to other model, endpoints, and study designs.

A major integrative assessment of the scientific literature concerning neurotoxicology and neuropharmacology have been evaluated within the context of dose response relationships. The findings indicate that the hormetic dose response relationship occurs with exceptional frequency and is highly generalizable being independent of biological model, endpoint measured and chemical class evaluated. These findings have potential implications with respect to drug discovery, drug development and clinical evaluation as well as inhuman toxicology and risk assessment. The completed findings have been subjected to peer-review and will be published in their entirety in 2008 within *Critical Review in Toxicology.*

International conferences were conducted on the toxicology and risk assessment implications of hormesis for chemicals and radiation. The conferences were conducted at the University of Massachusetts, Amherst Massachusetts in June 2005, 2006, and May 2007 with papers being published in the peer-reviewed journal *Dose-Response*.

**Transition/Technology Transfers:** None

**Changes in Research Objective:** N/A

**Change in Program Manager:** N/A

**Extensions Granted or Milestones Slipped:** N/A